Article 34

CLAIMS

1. Method for preparing, by filtration, a factor VIII solution which is virally secure and essentially devoid of high molecular weight vWF, according to which:

- a solution containing highly or very highly pure factor VIII is prepared, which is essentially devoid of high molecular weight factor VIII-vWF complexes;

- a step is carried out, of filtration of said solution which is essentially devoid of high molecular weight vWF-associated factor VIII through a hydrophilic filter having a porosity as low as 15 nm.

2. Method according to claim 1, characterized in that it also comprises, before the filtration step, a step which enables the dissociation of the high molecular weight factor VIII-vWF complexes and the production of a solution which is essentially devoid of high molecular weight vWF-associated factor VIII.

3. Method according to either of claims 1 or 2, characterized in that said dissociation step is carried out by means of a chaotropic ion in sufficient amount to enable the dissociation.

4. Method according to claim 3, characterized in that said chaotropic ion is a divalent ion.

5. Method according to claim 4, characterized in that said divalent ion is the Ca^{2+} ion.

6. Method according to one of claims 3 to 5, characterized in that said divalent ion is added in the form of a saline solution from 0.2 M to salt saturation.

7. Method according to claim 6, characterized in that said solution is a $CaCl_2$ solution.

8. Method according to either of claims 6 or 7, characterized in that said Ca^{2+} ion is added in the form of a $CaCl_2$ solution, 0.35 M to saturation.

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9. Method according to one of claims 1 to 8, characterized in that step b) is carried out at a pressure lower than the recommendation threshold recommended by the supplier.

10. Method according to claim 9, characterized in that said filter is a Planova® 15 N membrane used at a pressure lower than 0.3 bar, preferably lower than 0.2 bar.

11. Method according to one of claims 1 to 10, characterized in that step b) is carried out at a temperature of about 35±5°C.

12. Method according to any one of claims 1 to 11, characterized in that the starting solution is obtained by purification of a plasmatic fraction, in particular the cryoprecipitated fraction of the plasma, by ion exchange chromatography.

13. Method according to claim 12, characterized in that the concentrated factor VIII fraction obtained at the end of the purification by ion exchange chromatography is eluted under the dissociating conditions of step a).

14. Method according to one of claims 1 to 11, characterized in that the starting factor VIII solution is obtained by prepurification of a plasmatic fraction, in particular the cryoprecipitated fraction of the plasma, by heparin precipitation.

15. Method according to any one of claims 1 to 14, characterized in that the starting factor VIII solution is partially virally inactivated by solvent/detergent treatment.

16. Method according to one of claims 1 to 11, characterized in that the starting factor VIII solution comprises immunopurified factor VIII.

17. Method according to one of claims 1 to 11, characterized in that the starting factor VIII solution comprises recombinant factor VIII.

18. Method according to one of claims 1 to 17, characterized in that the factor VIII in the starting

solution has a specific activity at least equal to 50 IU/mg, preferably at least equal to 100 IU/mg.

19. Method according to any one of claims 1 to 18, characterized in that the factor VIII concentration C of the starting factor VIII solution is from approximately 2 to approximately 100 U/ml, preferably from approximately 10 to approximately 50 U/ml.

20. Method according to one of claims 1 to 19, characterized in that the protein content of the starting factor VIII solution is from approximately 0.05 to approximately 0.5 mg/ml, preferably from approximately 0.1 to approximately 0.5 mg/ml.

21. Virally secure factor VIII solution which can be obtained by the method according to any one of claims 1 to 20.

22. Solution according to claim 21, as a medicinal product.

23. Solution according to claim 22, as a medicinal product for treating hemophilia A.

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